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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/796,782	03/09/2004	George J. Brewer	4100.001099	1675

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EXAMINER	
MAIER, LEIGH C	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 05/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/796,782	BREWER ET AL.	
	Examiner	Art Unit	
	Leigh C. Maier	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40 and 80-122* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40 and 80-122* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/9/04, 11/22/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

S-O-O.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 44 and 90-115 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that Applicant, at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method of treatment comprising the administration of an agent, wherein the agent is described in terms of its function. A description in terms of function may be adequate when the functional characteristics are coupled with a known or disclosed with a known or disclosed correlation between function and structure or by a combination of such identifying characteristics, sufficient to demonstrate that Applicant was in possession of the claimed genus.

According to the MPEP §2163 I. A. "the issue of a lack of adequate written description may arise even for an original claim when an aspect of the claimed invention has not been described with sufficient particularity such that one skilled in the art would recognize that the applicant had possession of the claimed invention. The claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately

described in the specification and which is not conventional in the art or known to one of ordinary skill in the art." The MPEP states in §2163 II 3 ii) "The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice (see i)(A), above), reduction to drawings (see i)(B), above), or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus (see i)(C), above). See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406."

The Court of Appeals for the Federal Circuit held in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 at 1406. "[a] written description of an invention involving a chemical genus, like a description of a chemical species, "requires a precise definition, such as by structure, formula, [or] chemical name, "of the claimed subject matter sufficient to distinguish it from other materials. *In re Smythe*, 480 F.2d 1376, 1383, *Fiers* , 984 F.2d at 1171, 25 USPQ2d at 1606; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . ."). " Applicant's functional definitions in the claimed formula simply lack the precision required by the Court of Appeals for the Federal Circuit.

According to the MPEP §2163.02 Standard for Determining Compliance With the Written Description Requirement,

> "The courts have described the essential question to be addressed in a description requirement issue in a variety of ways. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed". *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter". *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting In *re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983))."

This case was filed before Applicants had a clear idea of the structures of their desired agents, other than the thiomolybdate derivatives particularly recited in the dependent claims, having the recited function or how to make those undescribed compounds. The examiner recognizes that it is not required that the patent to set forth the exact chemical structure of compounds in question, but "[i]t is only necessary that the patent set forth enough detail to allow a person of ordinary skill in the art to understand what is claimed and to recognize that the inventor invented what is claimed." See *University of Rochester v. G. D. Searle & Co.* 68 USPQ2d at 1432 (CAFC 2004). This requirement may be met by disclosing sufficiently detailed, relevant identifying characteristics when coupled with a known or disclosed *correlation between function and structure*. Now such correlation has been disclosed here. Other than the thiomolybdate derivatives, the specification discloses no assay for screening for such compounds or any guidance as to the possible structural elements that such agents would be likely to possess. The specification provides broad areas of future research and speculation, inviting undue experimentation in learning how to use Applicant's invention.

Applicants are reminded of what the U.S. Court of Appeals Federal Circuit wrote in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398, "In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus." "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See *Fiers*, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing Amgen). "It is only a definition of a useful result rather than a definition of what achieves that result." "The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.")".

Claims 44 and 80-115 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to the treatment of vascular diseases characterized by aberrant vascularization by the administration of an agent that binds copper and forms an agent-copper-

protein complex. The dependents are drawn to the use of thiomolybdate derivatives as the "agent."

Regarding the agent to be used, any method(s) for making agents other than thiomolybdate derivatives are not enabled due to lack of written description. This is addressed above.

With respect to the diseases to be treated, Brewer states in a post-filing publication: "Based on one pilot clinical trial, it seems unlikely that TM [tetrathiomolybdate] will be effective in macular degeneration. On the other hand, a positive retinopathy animal model study predicts that TM may be helpful therapy in diabetic retinopathy. We have no basis for prediction whether TM will be useful in other disease where neovascularization is a factor, such as psoriasis and rheumatoid arthritis." (J. Cell. Mol. Med., 2003 at page 17, 1st full paragraph.) The positive results for diabetic retinopathy are noted. However, retinal neovascularization is addressed further by Elner et al (IOVS, 2005, last paragraph of the reference). The reference states "TM significantly reduced neovascularization *only if used before its onset.*" (Emphasis added) Based on these findings, the examiner must conclude that the treatment of the recited diseases was not enabled at the time of filing.

Claims 116-122 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The claims appear to be enabled for the treatment of vascularization associated with cancer but not the other recited diseases.

Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

(1) The quantity of experimentation necessary (time and expense);
(2) The amount of direction or guidance presented;
(3) The presence or absence of working examples of the invention;
(4) The nature of the invention;
(5) The state of the prior art;
(6) The relative skill of those in the art;
(7) The predictability or unpredictability of the art; and
(8) The breadth of the claims.

Applicant has presented data demonstrating impressive results with respect to the treatment of cancer with the disclosed thiomolybdate derivatives and disclosed that the mechanism is based on the inhibition of angiogenesis. The claims are drawn to the treatment of a broad range of diseases wherein angiogenesis is implicated, but no data for diseases other than cancer has been disclosed. Moreover, based on finding by Brewer and Elner, as discussed above, the experimental results on the treatment of any non-cancer related aberrant vascularization have been negative. Although the relative skill of those in the art is likely to be high, the predictability of this art appears to be low. One of the Applicants, in fact, has addressed the question of predictability in this area. See Brewer, above. Based on the forgoing, it must be concluded that one of ordinary skill in the art would require undue experimentation at great expense to use the invention commensurate with the scope that is claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 116, 117, and 120 are rejected under 35 U.S.C. 102(a) as being anticipated by Merajver, et al (Proc. Angiogen. Cancer, 1998).

Merajver discloses the treatment of breast cancer in mice comprising the administration of tetrathiobolybdate. It is noted that a declaration in accordance with in re Katz was submitted during prosecution in the parent case (S.N. 09/389,435) to overcome this reference. Applicants are requested to re-submit this declaration in order to maintain a clear record of prosecution in the instant case.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 119 is rejected under 35 U.S.C. 103(a) as being unpatentable over Merajver, et al (Proc. Angiogen. Cancer, 1998), as applied to claims 116, 117, and 120 above.

Merajver teaches as set forth above. The reference does not exemplify the treatment of human subjects.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to administer TM to treat cancer in humans. One of ordinary skill would be motivated to provide such treatment because the reference had taught that good results were seen with a widely used mouse model. Therefore, one of ordinary skill would reasonably expect success in using the treatment with human subjects.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 44, 80, 83-85, 104, 106, 107, and 116-122 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 43-48 and 57 of U.S. Patent No. 6,703,050. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The instant claims are drawn to the treatment of a group of diseases associated with aberrant neovascularization by administration of by the administration of an agent that binds copper and forms an agent-copper-protein complex wherein the "agent" may be a thiomolybdate derivative. The claims of '050 are drawn to the treatment of wet-type macular degeneration, a disease associated with choroidal neovascularization, and one of the age-related types of macular degeneration. The treatment comprises adminstration of an agent that binds copper and forms an agent-copper-protein complex wherein the "agent" may be a thiomolybdate derivative. Therefore, the claims of '050 would anticipate the instant claims.

Claims 116, 117, 119, and 122 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 3, 15-18, and 36-42 of U.S. Patent No. 6,703,050. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The instant claims are drawn to the treatment of a group of diseases associated with aberrant neovascularization by administration of by the administration of an agent that binds copper and forms an agent-copper-protein complex wherein the "agent" may be a thiomolybdate derivative. The claims of '050 are drawn to the treatment of cancer using thiomolybdate derivatives. Therefore, the claims of '050 would anticipate the instant claims.

It is noted that in the remarks accompanying the instant filing, Applicant has indicated a willingness to file a terminal disclaimer if necessary.

Examiner's hours, phone & fax numbers

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (571) 272-0656. The examiner can normally be reached on Tuesday, Thursday, and Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson (571) 272-0661, may be contacted. The fax number for Group 1600, Art Unit 1623 is (703) 308-4556 or 305-3592.

Visit the U.S. PTO's site on the World Wide Web at http://**www.uspto.gov**. This site contains lots of valuable information including the latest PTO fees, downloadable forms, basic search capabilities and much more.

Leigh C. Maier

Leigh C. Maier
Primary Examiner
May 13, 2005

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